

**In the Specification:**

Please amend the specification as shown:

Please delete Table 1 on page 9 and replace it with the following Table:

**Table 1. Experimentally observed and calculated masses of preproinsulin derived peptides eluted from HLA-DR4, and their matching sequences**

Observed m/z	Calculated m/z	Mass accuracy (ppm)	Residues in preproinsu lin	Sequence	IC <sub>50</sub> for binding to HLA-DR4 ( $\mu$ M)
2336.970	2337.216	85.8	B27-C15	TPKTRREAEDLQVGQVELGGGP <b>(SEQ ID NO: 1)</b>	50
2305.312	2305.203	77.9	C3-C26	EDLQVGQVELGGGPGAGSLQPLAL <b>(SEQ ID NO: 2)</b>	3
2305.312	2305.203	77.9	C4-C27	D <b>L</b> QVGQVELGGGPGAGSLQPLALE <b>(SEQ ID NO: 3)</b>	3
1836.922	1836.981	32.3	C13-C32	GGGPGAGSLQPLALEGSLQK <b>(SEQ ID NO: 4)</b>	5
1865.546	1866.081	286.5	C19-A3	<b>(SEQ ID NO: 5)</b> GSLQPLALEGSLQKRGIV	0.5
1865.546	1866.044	267.0	C22-A5	<b>(SEQ ID NO: 6)</b> QPLALEGSLQKRGIVEQ	0.4
2224.543	2225.072	250.0	C25-A12	<b>(SEQ ID NO: 7)</b> ALEGSLQKRGIVEQCCTSICS	10

Proinsulin sequence:

B-chain	C-peptide	A-chain
FVNQHLCGSHLVEALYLVCGERGFFYTPKT	R-R EAEDLQVGQVELGGGPGAGSLQPLALEGSLQ	K-R GIVEQCCTSICSLYQLENYCN
<b>(SEQ ID NO: 8)</b>		

Notes: boxes delineate potential nested sets in which the amino acid in bold represents the most likely P1 residue; in the proinsulin sequence, the dibasic motifs R-R and K-R represent the cleavage sites for removal of C-peptide and these residues are subsequently removed by peptidases

Please delete the paragraph on page 10, lines 1-9 and replace it with the following paragraph:

The present invention comprises a peptide identified as indicated above and having a sequence comprising or consisting of QPLALEGSLQK **(SEQ ID NO: 9)**. Three peptides containing the above sequence are:

GGGPGAGSLQPLALEGSLQK **(SEQ ID NO: 4)**,  
 GSLQPLALEGSLQKRGIV **(SEQ ID NO: 5)**,  
 and QPLALEGSLQKRGIVEQ **(SEQ ID NO: 6)**

of which that having the sequence GSLQPLALEGSLQKRGIV **(SEQ ID NO: 5)** is highly preferred.

Please delete the paragraph on page 10, lines 11-12 and replace it with the following paragraph:

Various combinations of these peptides may be used, including a consensus sequence that covers all 3 of these, ie GGGPGAGSLQPLALEGSLQKRGIVEQ **(SEQ ID NO: 10)**.

Please delete Table 2 on page 10 and replace it with the following Table:

**Table 2. IA-2 peptides eluted from HLA-DR4 that have synergy with preproinsulin 75-92**

Numbering in IA-2	Sequence
709-36	LAKIEWQALCAYQAEPNTCATAQGEGNIK <b><u>(SEQ ID NO: 11)</u></b>
752-75	KLKVESSPSRSDYINASPPIEHDP <b><u>(SEQ ID NO: 12)</u></b>
853-72	SFYLKNVQTQETRSLTQFHF <b><u>(SEQ ID NO: 13)</u></b>

Please delete the paragraph on page 15, line 23, to page 16, line 12 and replace it with the following paragraph:

The following procedures are used.

Fresh heparinised blood was obtained from 25 Caucasian Type 1 DM patients with HLA-DR4 and acute onset of symptoms, requiring insulin from diagnosis, and from 14 non-diabetic healthy control subjects matched for age and HLA type. Peripheral blood mononuclear cells (PBMCs) were isolated fresh on density gradients (Lymphoprep, Nycom Pharma, Norway) and washed in RPMI 1640 (Life Technologies, Paisley, UK) twice before use. Fresh PBMCs in RPMI 1640 supplemented with antibiotics (TC medium; all Life Technologies) and 10% human AB serum (Harlan SeraLab, Leicestershire, UK) were dispensed into 48-well plates at a density of  $2 \times 10^6$  in 0.5ml supplemented with peptide to a final concentration of  $10 \mu\text{M}$  and incubated at  $37^\circ\text{C}$ , 5%  $\text{CO}_2$ , tilted by  $5^\circ$ . Positive control wells comprised TC medium containing an equivalent concentration of peptide diluent alone (DMSO), tetanus toxoid (final concentration 100ng/ml), or PMA/ionomycin (5ng/ml and 745 ng/ml final concentrations, respectively). Negative control wells comprised TC medium containing DMSO alone, or supplemented with equivalent concentrations of the following control peptides; the promiscuous HLA-DR binding MHC class II invariant chain peptide, residues 98-117 PKPPKPVSKMRMATPLLMQA (**SEQ ID NO: 14**); and three non-autoantigenic peptides from the coxsackievirus B4 P2C protein 55-75 LLESQIATIEQSAPSQSDQEQ (**SEQ ID NO: 15**), 133-154 AGKSVATNLIGRSLAEKLNSSV (**SEQ ID NO: 16**) and 191-213 CQMVSSVDFVPPMAALEEKILF (**SEQ ID NO: 17**) identified as having good binding properties for HLA-DR4 ( $\text{IC}_{50}$  values 8.2, 2.1 and  $0.3 \mu\text{M}$  respectively).